STIC Search Report
EIC 3700

STIC Database Tracking Number: 146974

TO: Samuel Gilbert **Location: RND 7a25** **Art Unit: 3736** 3/18/05 **Case Serial Number: 10/705989**	**From: Jeanne Horrigan** **Location: RND 8A34** **Phone: 571-272-3529** **jeanne.horrigan@uspto.gov**

Search Notes

Attached are the search results for the method of treating remodeling.

I tagged the references that I thought were most useful, but I suggest that you review ALL of the results.

Also attached is a search feedback form. Completion of the form is voluntary. Your completing this form would help us improve our search services.

I hope the attached information is useful. Please feel free to contact me if you have any questions or need additional searching on this application.

JH

Access DB# 146974

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Samuel Gilbert Examiner #: 70632 Date: 3/7/05
Art Unit: 3736 Phone Number 272-4725 Serial Number: 10/705,889
Mail Box and Bldg/Room Location: Rnd 325 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Expandable Cardiac Harness for treating Congestive Heart failure

Inventors (please provide full names): Lillip Lau ; Bill Hartigan

Earliest Priority Filing Date: 3/10/2000

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

method of treating a heart (treating reverse remodeling)
- placing an elastic jacket (harness) on the heart
- providing elastic resistance to stretch during diastole and contractile augmentation during systole.

must *

- decreasing elastic resistance as reverse remodeling occurs

not needed for all methods

Received 3/7/05 11:15a DS

****

STAFF USE ONLY

Searcher: Jeanne Bomgaars
Searcher Phone #: 23529
Searcher Location:
Date Searcher Picked Up:
Date Completed: 3/18/05
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time:

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

STIC Search Results Feedback Form

EIC 3700

Questions about the scope or the results of the search? Contact ***the EIC searcher or contact*:**

John Sims, EIC 3700 Team Leader
RND 8B35, Phone 2-3507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 3730*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/EIC3700 RND 8B31

Search and Information Resources Administration

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File 149:TGG Health&Wellness DB(SM) 1976-2005/Mar W1
         (c) 2005 The Gale Group
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         (c) 2005 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2005/Mar 18
         (c)2005 The Gale Group
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         (c) 2005 The HW Wilson Co.
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File 441:ESPICOM Pharm&Med DEVICE NEWS 2005/Feb W2
         (c) 2005 ESPICOM Bus.Intell.
Set     Items   Description
S1      63106   REMODELING
S2    3084916   REVERS??? OR TREAT? OR PREVENT?
S3     600532   HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-
             CARDI? OR EPICARDI?
S4      12176   DIASTOLE OR DIASTOLIC
S5    2963235   RESIST? OR LIMIT???
S6    3701568   STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-
             LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7       8002   SHAPE(1N)CHANG???
S8    3540727   SYSTOLE OR SYSTOLIC OR CONTRACT???
S9    3666930   AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10    174139   HARNESS OR HARNESSES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? -
             OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11    570015   BIND??? OR BOUND OR CONSTRAINT? ?
S12    123878   GIRDLING OR WRAP? ?
S13      2204   DISTEND???
S14       134   S2(1W)S1
S15        27   S10:S12 AND S14
S16        22   (S4:S9 OR S13) AND S15
S17        19   RD (unique items)
S18         3   S17/2001
S19         2   S17/2002
S20         6   S17/2003
S21         1   S17/2004:2005
S22         7   S17 NOT S18:S21
S23         7   Sort S22/ALL/PD,A [not relevant]
S24         5   S15 NOT S16
S25         3   RD (unique items) [not relevant]
S26        30   S1(S)S3(S)S10:S12
S27        27   S26 NOT S15
S28        21   RD (unique items)
S29         3   S28/2001
S30         4   S28/2002
S31         1   S28/2003
S32         3   S28/2004:2005
S33        10   S28 NOT S29:S32
S34        10   Sort S33/ALL/PD,A [not relevant]
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S35      68073   S10/TI,DE OR S11/TI,DE OR S12/TI,DE
S36          1   S14 AND S35 [not relevant]

File  20:Dialog Global Reporter 1997-2005/Mar 18
         (c) 2005 The Dialog Corp.
Set      Items   Description
S1       15725   REMODELING
S2     3190824   REVERS??? OR TREAT? OR PREVENT?
S3      819914   HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-
              CARDI? OR EPICARDI?
S4         866   DIASTOLE OR DIASTOLIC
S5     2974893   RESIST? OR LIMIT???
S6     2693066   STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-
              LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7        5647   SHAPE(1N)CHANG???
S8     3069233   SYSTOLE OR SYSTOLIC OR CONTRACT???
S9     4004079   AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10     197942   HARNESS OR HARNESSES OR JACKET? ?*OR SOCK? ? OR GIRDLE? ? -
              OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11     532953   BIND??? OR BOUND OR CONSTRAINT? ?
S12     118465   GIRDLING OR WRAP? ?
S13        955   DISTEND???
S14         33   S2(1W)S1
S15          6   S10:S12 AND S14
S16          5   RD (unique items) [not relevant]
S17         27   S14 NOT S15
S18         24   RD (unique items)
S19         19   S18/2001:2005
S20          5   S18 NOT S19 [not relevant]

File 155:MEDLINE(R) 1951-2005/Mar W2
         (c) format only 2005 The Dialog Corp.
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         (c) 2005 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File  94:JICST-EPlus 1985-2005/Feb W1
         (c)2005 Japan Science and Tech Corp(JST)
File  95:TEME-Technology & Management 1989-2005/Feb W1
         (c) 2005 FIZ TECHNIK
File  99:Wilson Appl. Sci & Tech Abs 1983-2005/Feb
         (c) 2005 The HW Wilson Co.
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         (c) 2005 INIST/CNRS
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         (c) 2005 Elsevier Eng.  Info. Inc.
File   2:INSPEC 1969-2005/Mar W1
         (c) 2005 Institution of Electrical Engineers
File  35:Dissertation Abs Online 1861-2005/Feb
         (c) 2005 ProQuest Info&Learning
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File  65:Inside Conferences 1993-2005/Mar W2
        (c) 2005 BLDSC all rts. reserv.
Set     Items   Description
S1     124575   REMODELING
S2   14843278   REVERS??? OR TREAT? OR PREVENT?
S3    3244407   HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-
            CARDI? OR EPICARDI?
S4     252080   DIASTOLE OR DIASTOLIC
S5    7041231   RESIST? OR LIMIT???
S6    4375014   STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-
            LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7      38710   SHAPE(1N)CHANG???
S8    1218962   SYSTOLE OR SYSTOLIC OR CONTRACT???
S9    4476340   AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10     67360   HARNESS OR HARNESSES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? -
            OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11   4769970   BIND??? OR BOUND OR CONSTRAINT? ?
S12     15765   DISTEND???
S13     17925   GIRDLING OR WRAP? ?
S14      1743   S2(1W)S1
S15    956740   ELASTIC?
S16        37   (S10 OR S13) AND S14
S17       110   S11 AND S14
S18        67   S16:S17 AND  (S4 OR S8 OR S15)
S19        24   RD (unique items)
S20        12   S19/2001:2003
S21         4   S19/2004:2005
S22         8   S19 NOT S20:S21
S23         8   Sort S22/ALL/PY,A
S24     74116   S5(1W)S6:S7
S25        17   S5(1W)S12
S26      3235   8(1N)S9
S27         0   S S8(1N)S9
S28     28252   S8(1N)S9
S29         8   S14 AND (S10 OR S13) AND (S24 OR S25 OR S28)
S30         0   S29 NOT S18
S31         7   S14 AND S11 AND (S24 OR S25 OR S28)
S32         0   S31 NOT S18
S33       723   S1 AND (S10 OR S11 OR S13) AND (S15 OR S4 OR S8 OR S24 OR -
            S25 OR S28)
S34       364   S3 AND S33
S35       169   S1/TI,DE AND S34
S36       135   S35 NOT S18
S37        94   RD (unique items)
S38        27   S37/2001:2002
S39        32   S37/2003:2005
S40        35   S37 NOT S38:S39
S41        35   Sort S40/ALL/PY,A

23/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.

0009553926   BIOSIS NO.: 199598021759
 Reverse   remodeling : Chronic effects of cardiomyoplasty in failing human
  heart and role of external  constraint
```

AUTHOR: Kass David A; Pak Peter H; Baughman Kenneth L; Cho Peter; Acker Michael
AUTHOR ADDRESS: Johns Hopkins Med. Inst., Baltimore, MD, USA**USA
JOURNAL: Circulation 90 (4 PART 2): pI112 1994 1994
CONFERENCE/MEETING: 67th Scientific Sessions of the American **Heart** Association Dallas, Texas, USA November 14-17, 1994; 19941114
ISSN: 0009-7322
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

23/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10948295 PMID: 7729016
Reverse remodeling from cardiomyoplasty in human **heart** failure. External **constraint** versus active **assist**.
Kass D A; Baughman K L; Pak P H; Cho P W; Levin H R; Gardner T J; Halperin H R; Tsitlik J E; Acker M A
Division of Cardiology, Johns Hopkins Medical Institutions, Baltimore, Md 21287, USA.
Circulation (UNITED STATES) May 1 1995, 91 (9) p2314-8, ISSN 0009-7322 Journal Code: 0147763
Contract/Grant No.: HL-47511; HL; NHLBI; RR00035; RR; NCRR
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND: Cardiomyoplasty (CM) is a novel surgical therapy for **dialted** cardiomyopathy. In this procedure, the latissimus dorsi muscle is **wrapped** around the **heart** and chronically paced synchronously with **ventricular systole** . While studies have found symptomatic improvement from this therapy, the mechanisms by which CM confers benefit remain uncertain. This study sought to better define these mechanisms by means of serial pressure-volume relation analysis. METHODS AND RESULTS: Serial pressure-volume studies were performed by the conductance catheter method in three patients (total to date) with **dialted** cardiomyopathy (New York **Heart** Association class III) who underwent CM. Data were measured at baseline (before surgery) and at 6 and 12 months after CM. Chronic left **ventricular** (LV) **systolic** and **diastolic changes** induced by CM were evaluated with the stimulator in its stable pacing mode (every other beat) and after temporarily suspending pacing. CM-stimulated beats were compared with pacing-off beats to evaluate active **systolic assist** effects of CM. In each patient, CM resulted in a chronic lowering of **cardiac** end-**diastolic** volume and an increased ejection fraction. Most notably, the end- **systolic** pressure-volume relation shifted leftward, consistent with **reversal** of chronic chamber **remodeling**. In contrast, the **diastolic** pressure-volume relation was minimally altered, and the loops shifted down along the same baseline relation. These marked chronic **changes** in LV function measurable with CM stimulation off contrasted to only minor acute effects observed when the muscle **wrap** was activated. This suggests that the benefit of CM derived less from active **systolic assist** than from **remodeling**, perhaps because of an external elastic **constraint** .

CONCLUSIONS: These data, while **limited** to a small number of patients, suggest that CM can **reverse remodeling** of the **dialted** failing **heart**. While **systolic** squeezing **assist** effects of CM may play a role in some patients, our study found that this was not required to achieve substantial benefits from the procedure. We speculate that CM may act more passively, like an elastic **girdle** around the **heart**, to help **reverse** chamber **remodeling** .
Record Date Created: 19950601
Record Date Completed: 19950601

23/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11671823 PMID: 9064980
[Dynamic cardiomyoplasty: current status and concepts of the mechanism of action]
Dynamische Kardiomyoplastik: Aktueller Stand und Vorstellungen zum Wirkungsmechanismus.
Lange R; Hagl S
Abt. Herzchirurgie Chirurgische Universitatsklinik, Heidelberg.
Zeitschrift fur Kardiologie (GERMANY) 1996, 85 Suppl 6 p309-15, ISSN 0300-5860 Journal Code: 0360430
Publishing Model Print
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Surgical **treat**ment of end-stage **heart** failure offers **heart** transplantation as a well established and effective **treat**ment option. In addition, the permanent implantation of left-**heart assist**-devices is now gaining increasing importance. Yet, both methods also have inherent drawbacks and may not be available to all patients, so that new methods are constantly evaluated. Cardiomyoplasty was introduced into clinical practice 10 years ago, but still lacks general acceptance as a routine method. Worldwide results show a considerable symptomatic improvement with only small effects on **systolic cardiac** function. Survival rate was significantly improved by careful patient selection. As a mechanism of action the skeletal muscle **wrap** exerts some active improvement of **systolic** wall motion of the **heart**/skeletal muscle-complex. However, probably more important is an acute and chronically persisting shift of the pressure-volume relation to the left. This process results in a " **reverse remodeling** " of the insufficient **heart** with an improvement of the "**contract**ility reserve". Cardiomyoplasty is indicated in patients with contraindications to **heart** transplantation and as a bridge-to-transplantation in patients with **ventricular** arrhythmia and severely impaired left **ventricular** function, concomitant with ICD implantation. (25 Refs.)
Record Date Created: 19970319
Record Date Completed: 19970319

23/7/5 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

07341272 EMBASE No: 1998245552
Remodeling of **cardiac** membranes during the development of congestive **heart** failure
Dhalla N.S.; Shao Q.; Panagia V.
Dr. N.S. Dhalla, Institute of Cardiovascular Sciences, St. Boniface Gen. Hosp. Res. Center, 351 Tache Avenue, Winnipeg, Man. R2H 2A6 Canada
Heart Failure Reviews (**HEART** FAIL. REV.) (Netherlands) 1998, 2/4 (261-272)
CODEN: HFREF ISSN: 1382-4147
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 125

Various proteins such as Casup 2sup + channels, Casup 2sup +-pump ATPase, Nasup +- Casup 2sup + ex**changer**, and Nasup +-Ksup + ATPase in the sarcolemmal (SL) membrane are considered to be intimately involved in Casup 2sup +-influx and Casup 2sup +-efflux processes in the cardiomyocyte. On the other hand, Casup 2sup +-pump ATPase, Casup 2sup +-release channels, Casup 2sup +-regulatory protein (phospholamban), and Casup 2sup +- **binding** protein (calsequestrin) in the sarcoplasmic reticulum (SR) are known to participate in raising and lowering the intracellular concentration of Casup 2sup + for the occurrence of **cardiac** **contraction** and relaxation processes. Therefore, a defect in any of the SL and SR proteins can be seen to result in Casup 2sup +-handling abnormalities in cardiomyocytes and subsequently in **cardiac** dysfunction during the development of **heart** failure. In this review, evidence is presented to show that **changes** in the expression of genes specific for **cardiac** membrane proteins may lead to **remodeling** of both SR and SL membranes during the development of **heart** failure. Although a great deal of work on **changes** in gene expression for the SR membrane proteins has been carried out in the failing **heart**, relatively little information regarding **changes** in gene expression for SL proteins has appeared in the literature. **Prevention** of **remodeling** of **cardiac** membranes by modification of **changes** in the gene expression is suggested to serve as an important target for the **treatment** of **heart** failure.

23/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12263795 PMID: 9573504
Surgical approaches to arresting or **reversing** chronic **remodeling** of the failing **heart**.
Kass D A
Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21287, USA.
Journal of **cardiac** failure (UNITED STATES) Mar 1998, 4 (1) p57-66, ISSN 1071-9164 Journal Code: 9442138
Publishing Model Print
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Chronic **ventricular remodeling** is a central feature of **heart** failure that strongly correlates with a poor prognosis. Several recent surgical **treat**ments for **heart** failure may derive benefit by their ability to arrest or substantially **reverse** this **remodeling** process. Dynamic cardiomyoplasty involves **wrap**ping the **heart** with the latissimus dorsi muscle and stimulating the muscle to **assist contraction** . The **wrap** itself may provide a **constraint** helping to **limit** progressive **cardiac dialtion** and/or **assist** in **reversing** this process. Left **ventricular assist** devices almost completely unload the **heart** and **augment** systemic circulation, thereby reducing neurohumoral activation. These combined effects seem to alter the chamber and cellular phenotype, and **reversal** of some molecular **change**s are associated with failure. Lastly, the partial ventriculectomy procedure directly **reverse**s **remodeling** by acute removal of a portion of the lateral wall. Only preliminary nonrandomized trial data are currently available for each of these therapies with larger trials under way. However, early results are intriguing and are yielding insights into these mechanisms. (63 Refs.)
Record Date Created: 19980702
Record Date Completed: 19980702

41/7/10 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

06636461 EMBASE No: 1996301273
Mechanisms of dynamic cardiomyoplasty: Current concepts
Oh J.H.; Badhwar V.; Chiu R.C.-J.
Montreal General Hospital, 1650 Cedar Avenue,Montreal, Que. H3G 1A4 Canada
Journal of **Cardiac** Surgery (J. CARD. SURG.) (United States) 1996, 11/3 (194-199)
CODEN: JCASE ISSN: 0886-0440
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Dynamic cardiomyoplasty is an operation that is undergoing worldwide clinical evaluation. It had been developed to utilize the patient's own skeletal muscle to **assist** the failing **heart** . Although the clinical and quality of life benefits of cardiomyoplasty have been reported in most patients, the results of quantitative hemodynamic analyses have been less consistent. This has prompted the reevaluation of the mechanisms of dynamic cardiomyoplasty other than simple **cardiac** compression by the **wrapped** muscle. There is good evidence to suggest that the following, either together or in part, comprise some of the mechanisms of dynamic cardiomyoplasty: (1) direct **systolic assist** ; (2) myocardial (wall stress) sparing effect; (3) **remodeling** / **girdling** effect; and (4) angiogenesis. Current concepts and potential additional mechanisms are discussed and integrated, based on a review of the literature and our own recent studies.

41/7/11 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05299389 Genuine Article#: VN754 Number of References: 156
Title: MEDICAL THERAPY CAN IMPROVE THE BIOLOGICAL PROPERTIES OF THE CHRONICALLY FAILING **HEART** - A NEW ERA IN THE **TREAT**MENT OF **HEART** -FAILURE
Author(s): EICHHORN EJ; BRISTOW MR
Corporate Source: UNIV TEXAS,VET ADM MED CTR,**CARDIAC** CATHETERIZATLAB IIIA2,4500 S LANCASTER/DALLAS//TX/75216; UNIV TEXAS,SW MED CTR,DEPT INTERNAL MED,DIV CARDIOL/DALLAS//TX/00000; UNIV COLORADO,HLTH SCI CTR,DIV CARDIOL/DENVER//CO/80262; UNIV TEXAS,VET ADM MED CTR,**CARDIAC** CATHETERIZATLAB IIIA2/DALLAS//TX/75216
Journal: CIRCULATION, 1996, V94, N9 (NOV 1), P2285-2296
ISSN: 0009-7322
Language: ENGLISH Document Type: REVIEW
Abstract: Myocardial failure has been considered to be an ir**revers**ible and progressive process characterized by **Ventricular** enlargement, chamber geometric alterations, and diminished pump performance. However, more recent evidence has suggested that certain types of medical therapy may lead to retardation and even **revers**al of the cardiomyopathic process. In the failing **heart** , long-term neurohormonal/autocrine-paracrine activation results in abnormalities in myocyte growth, energy production and utilization, calcium flux, and receptor regulation that produce a progressively dysfunctional, mechanically inefficient **heart** . Interventions such as ACE inhibition and beta-blockade result in a reduction in the harmful long-term consequences of neurohormonal/autocrine-paracrine effects and retard the progression of left **ventricular** dysfunction or **ventricular remodeling** . Furthermore, in subjects with idiopathic **dial**ted or ischemic cardiomyopathy, antiadrenergic therapy with beta-blocking agents appears to be able to partially **reverse systolic** dysfunction and **ventricular remodeling** . Although the precise mechanisms underlying this latter effect have not yet been elucidated, the general mechanism appears to be via improvement in the biological function of the **cardiac** myocyte. Such an improvement in the intrinsic defect(s) responsible for myocardial failure will likely translate into important clinical benefits.

41/7/15 (Item 15 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05719393 Genuine Article#: WT449 Number of References: 17
Title: Dynamic cardiomyoplasty: Insights into the mechanisms of its success
Author(s): Patel HJ; Lankford EB; Polidori DJ; Pilla JJ; Acker MA (REPRINT)
Corporate Source: HOSP UNIV PENN,DIV CARDIOTHORAC SURG, 34TH & SPRUCE ST, SILVERSTEIN 6/PHILADELPHIA//PA/19104 (REPRINT); UNIV PENN,SCH MED, DEPT SURG/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED, DEPT MED/PHILADELPHIA//PA/19104
Journal: BASIC AND APPLIED MYOLOGY, 1997, V7, N1, P5-7
ISSN: 1120-9992 Publication date: 19970000
Publisher: UNIPRESS PADOVA, 231 VIA C BATTISTI, 35123 PADOVA, ITALY
Language: English Document Type: ARTICLE
Abstract: Dynamic cardiomyoplasty is a recently developed operation for the **treat**ment of end-stage **heart** failure. Recent studies have focused on the potential mechanism by which it may work. We have shown in a canine

model of **heart** failure, using transformed muscle, that CMP has at least two mechanisms. First, it stabilizes **ventricular** function and volumes chronically by a **girdl**ing mechanism. Secondly, dynamic **assist**ance acts acutely to **augment** **systolic** **contract**ion . These two mechanisms act to stabilize **cardiac** function and may potentially allow for **revers**al of the chronic **remodeling** process seen with progressive **heart** failure.

41/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12097096 PMID: 9396469
Stabilization of chronic **remodeling** by asynchronous cardiomyoplasty in **dilat**ed cardiomyopathy: effects of a conditioned muscle **wrap** .
Patel H J; Polidori D J; Pilla J J; Plappert T; Kass D; St John Sutton M; Lankford E B; Acker M A
Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.
Circulation (UNITED STATES) Nov 18 1997, 96 (10) p3665-71, ISSN 0009-7322 Journal Code: 0147763
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND: Dynamic cardiomyoplasty is a promising new therapy for **dilat**ed cardiomyopathy. The **girdl**ing effects of a conditioned muscle **wrap** alone have recently been postulated to partly explain its mechanism. We investigated this effect in a canine model of chronic **dilat**ed cardiomyopathy. METHODS AND RESULTS: Twenty dogs underwent rapid **ventricular** pacing (RVP) for 4 weeks to create a model of **dilat**ed cardiomyopathy. Seven dogs were then randomly selected to undergo subsequent cardiomyoplasty, and all dogs had 6 weeks of additional RVP. The cardiomyoplasty group also received 6 weeks of concurrent skeletal muscle stimulation consisting of single twitches delivered asynchronously at 2 Hz to transform the **wrap** without active **assist**ance. All dogs were studied by pressure-volume analysis and echocardiography at baseline and after 4 and 10 weeks of pacing. **Systolic** indices, including ejection fraction (EF), end- **systolic** elastance (Ees), and preload-recruitable stroke work (PRSW) were all increased at 10 weeks in the **wrap** versus controls (EF, 34.0 versus 27.1, P=.008; Ees, 1.65 versus 1.26, P=.09; PRSW, 35.9 versus 25.5, P=.001). **Ventricular** volumes, **diastolic** relaxation, and left **ventricular** end- **diastolic** pressures stabilized in the cardiomyoplasty group but continued to deteriorate in controls. Both the end- **systolic** and end- **diastolic** pressure-volume relationships shifted farther rightward in controls but remained stable in the cardiomyoplasty group. CONCLUSIONS: In addition to potential benefits from active **systolic** **assist**ance , benefits from dynamic cardiomyoplasty appear to be partially accounted for by the presence of a conditioned muscle **wrap** alone. This conditioned **wrap** stabilizes the **remodeling** process of **heart** failure, arresting progressive deterioration of **systolic** and **diastolic** function.
Record Date Created: 19980109
Record Date Completed: 19980109

41/7/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13504431 PMID: 10475482
Dynamic cardiomyoplasty: at the crossroads.
Acker M A
Division of Cardiothoracic Surgery, University of Pennsylvania School of Medicine, Philadelphia, USA. macker@mail.med.upenn.edu
Annals of thoracic surgery (UNITED STATES) Aug 1999, 68 (2) p750-5, ISSN 0003-4975 Journal Code: 15030100R
Publishing Model Print
Document type: Clinical Trial; Clinical Trial, Phase III; Journal Article ; Randomized Controlled Trial; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND: Dynamic cardiomyoplasty remains a promising, but still unproven surgical **treat**ment for patients with end-stage **heart** failure. Lack of a clear survival advantage and ongoing misunderstanding of its mechanism of action have hindered its acceptance as a **treat**ment alternative for patients with end-stage **heart** failure. This review seeks to update current clinical results and practice of dynamic cardiomyoplasty and to present its likely mechanism of action. METHODS: The method involved a literature review. RESULTS: More than 600 patients have undergone dynamic cardioplasty since 1985. Improvement in average New York **Heart** Association class was noted in 80% to 85% of hospital survivors. Operative mortality has decreased from 31% in Phase I to less than 3% in the ongoing Phase III trial. Clinical work as well as recent animal work supports the hypothesis that through a combination of long-term elastic **constraint** and active dynamic **assist**, dynamic cardiomyoplasty decreases myocardial wall stress associated with the **remodeling** process of progressive **heart** failure. CONCLUSIONS: Though dynamic cardiomyoplasty can be shown to **limit** the **remodeling** process of **heart** failure in animal studies and some patients, its ultimate role in the **treat**ment of **heart** failure will depend on the outcome of randomized, controlled studies. (38 Refs.)
Record Date Created: 19990915
Record Date Completed: 19990915

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File 350:Derwent WPIX 1963-2005/UD,UM &UP=200518
         (c) 2005  Thomson Derwent
File 347:JAPIO Nov 1976-2004/Nov(Updated 050309)
         (c) 2005 JPO & JAPIO
Set     Items   Description
S1       2695   REMODELING
S2    4353257   REVERS??? OR TREAT? OR PREVENT?
S3      45305   HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-
             CARDI? OR EPICARDI?
S4       1569   DIASTOLE OR DIASTOLIC
S5    2203483   RESIST? OR LIMIT???
S6     763502   STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-
             LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7      10077   SHAPE(1N)CHANG???
S8     109891   SYSTOLE OR SYSTOLIC OR CONTRACT???
S9    1043703   AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10     85261   HARNESS OR HARNESSES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? -
             OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11    435728   BIND??? OR BOUND OR CONSTRAINT? ?
S12     41578   GIRDLING OR WRAP? ?
S13      1316   DISTEND???
S14         6   S2(1W)S1 AND S10:S12
S15      1417   S10:S12(S)S3
S16        24   S4 AND S8 AND S15
S17        23   S16 NOT S14
S18      9490   S5(1N)(S6:S7 OR S13)
S19      1301   S9(1N)S8
S20    458759   ELASTIC?
S21        11   S15 AND S18:S19
S22         6   S21 NOT (S14 OR S16)
S23        18   S20(S)S15
S24        14   S23 NOT (S14 OR S16 OR S21)

14/34/6     (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.

012814036    **Image available**
WPI Acc No: 1999-620267/199953
  Method of implanting a long term cardiac support device in a pericardial
  sac for a failing heart
Patent Assignee: SNYDERS R V (SNYD-I); CARDIO TECHNOLOGIES INC (CARD-N)
Inventor: SNYDERS R V
Number of Countries: 086  Number of Patents: 006
Patent Family:
Patent No      Kind   Date     Applicat No     Kind   Date      Week
WO 9952470      A1  19991021  WO 99US7726      A   19990409  199953  B
AU 9932223      A   19991101  AU 9932223       A   19990409  200013
US 6095968      A   20000801  US 9881286       P   19980410  200039
                              US 99288488      A   19990408
JP 2002511305   W   20020416  WO 99US7726      A   19990409  200242
                              JP 2000543083    A   19990409
AU 758285       B   20030320  AU 9932223       A   19990409  200329
MX 2000009927   A1  20020401  WO 99US7726      A   19990409  200363
                              MX 20009927      A   20001010
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Priority Applications (No Type Date): US 9881286 P 19980410; US 99288488 A 19990408

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9952470	A1	E	19	A61F-002/04	
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
AU 9932223	A				Based on patent WO 9952470
US 6095968	A			A61M-001/12	Provisional application US 9881286
JP 2002511305	W		17	A61F-002/04	Based on patent WO 9952470
AU 758285	B			A61F-002/04	Previous Publ. patent AU 9932223 Based on patent WO 9952470
MX 2000009927	A1			A61F-002/04	Based on patent WO 9952470

Abstract (Basic): WO 9952470 A1

NOVELTY - Method of implanting a long term **cardiac** support in a **pericardial** sac includes enclosing a **heart** within the **pericardial** sac with the support device having an outer inelastic ply and an inner lining ply which abuts the **ventricular** masses of the **heart**; instilling a viscous fluid between the inelastic ply and the elastic lining ply; and monitoring the pressure of the viscous fluid in the device.

USE - The invention is useful for individuals suffering from certain late-stage **heart** failure disease entities, e.g. **dialted** cardiomyopathies.

ADVANTAGE - Diminutive fabrication features of the device showed that it is quite easily adjustable to any **cardiac** size and is virtually self-sizing relative to circumferential dimension requirements even for the very largest **hearts** for insertion around the **heart** and inside the **pericardial** sac. Subsequent filling of the sac space with a viscous silicone or other equivalent non-compressible fluid through the fill line of the device results in a viscous cardioplasty reinforcement of the thinned **ventricular** walls resulting to a reduction in LV and RV diameters to effect a desirable reduction of wall stress, which consequently provides for an effective **reverse remodeling** of the **heart** via both **diastolic** and **systolic** volumetric restriction but not constriction of the **ventricular** anatomy and with a subsequent improved physiological benefit to **cardiac** function.

DESCRIPTION OF DRAWING(S) - The figure is a frontal perspective view showing the entire **heart** and great vessels with the right and left **ventricles** enveloped by the **Ventricular Assist** Device **jacket** closely fitted within the **pericardial** sac.

Device (10)
Inelastic elastomeric biocompatible material (12)
Conduit fill line (7)
Pericardial sac (19)
pp; 19 DwgNo 5/5

Technology Focus:

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Device: The inelastic ply is adjustable to facilitate circumferential fitting of the device to the **heart**. The device has a diminutive structural dimension so that the **pericardial** sac can be saved with an ideally congruent fit of the device within the **pericardial** sac which allows a

free choice of closure of the **pericardial** sac. The device further includes a conduit fill line, an implantible reservoir having a junction with the conduit fill line, an adapter syringe attached to a fluid reservoir and to the conduit fill line, and an operable valve in the junction of the flexible reservoir and the fill line for charging fluid from the reservoir to the device.

Preferred Method: No or minimal pressurization in the device is registered with the result of a viscous cardioplasty reinforcement of the **ventricular** wall with a resultant reduction in left and right **ventricular** diameters and volumes to effect reduction of wall stress, thus effectively **remodeling** the **diastolic** and **systolic** volumetric character of the **heart** anatomy. The viscous fluid is instilled in simple gravity fill without requiring any superseding pressure. Minimal pressurization of 2-10 mmHg is developed within the device above the gravity fill at atmospheric pressure. A fluid reservoir for the fluid fill is provided and implanted in the upper abdominal subcutaneous space for refilling of the device. The fluid fill line includes a flexible portion to allow free positioning of the fill line. The device may be filled by a syringing flow from an external viscous fluid container and the fill line is plugged for revisiting in the subcutaneous site.

POLYMERS - Preferred Fluid: The viscous fluid is a high viscosity silicone biocompatible liquid preferably polydimethylsilicone, fluoropropylsilicone, or equivalent high viscosity fluid of similar density. The viscous fluid has a specific gravity of 0.97 or 0.98.

Derwent Class: A26; A96; D22; P32; P34
International Patent Class (Main): A61F-002/04; A61M-001/12

17/26,TI/15 (Item 15 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013908399
WPI Acc No: 2001-392612/200142
Left- **ventricular** sack for pumping blood from left- **ventricular** section in artificial-organ development, comprises an elastic rubber cord which spirally **wraps** periphery of sack main body in the form of a shell

17/34/20 (Item 20 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013011018 **Image available**
WPI Acc No: 2000-182870/200016
Trans**ventricular** splint for reducing wall stress of failing **heart** has elongate tension member of specified length with atraumatic anchors at each end
Patent Assignee: MYOCOR INC (MYOC-N)
Inventor: KEITH P T; MORTIER T J; PAULSON T M; SCHWEICH C J; VIDLUND R M
Number of Countries: 087 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200006026	A2	20000210	WO 99US16874	A	19990727	200016	B
US 6045497	A	20000404	US 97778277	A	19970102	200024	
			US 97933456	A	19970918		

			US 98124286	A	19980729	
AU 9952308	A	20000221	AU 9952308	A	19990727	200029
US 6261222	B1	20010717	US 97778277	A	19970102	200142
			US 97933456	A	19970918	
			US 98124286	A	19980729	
			US 2000497118	A	20000203	
EP 1143858	A2	20011017	EP 99937483	A	19990727	200169
			WO 99US16874	A	19990727	
US 6629921	B1	20031007	US 97778277	A	19970102	200374
			US 97933456	A	19970918	
			US 98124286	A	19980729	
			US 2000497118	A	20000203	
			US 2000697711	A	20001027	

Priority Applications (No Type Date): US 98124286 A 19980729; US 97778277 A 19970102; US 97933456 A 19970918; US 2000497118 A 20000203; US 2000697711 A 20001027

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200006026	A2	E	46	A61B-017/00	
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
US 6045497	A			A61B-017/12	CIP of application US 97778277 CIP of application US 97933456
AU 9952308	A				Based on patent WO 200006026
US 6261222	B1			A61M-031/00	CIP of application US 97778277 CIP of application US 97933456 Cont of application US 98124286 CIP of patent US 5961440 Cont of patent US 6045497 CIP of patent US 6050936
EP 1143858	A2	E		A61B-017/00	Based on patent WO 200006026
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
US 6629921	B1			A61M-031/00	CIP of application US 97778277 CIP of application US 97933456 Cont of application US 98124286 Cont of application US 2000497118 CIP of patent US 5961440 Cont of patent US 6045497 CIP of patent US 6050936

Abstract (Basic): WO 200006026 A2

NOVELTY - The trans**ventricular** splint has an elongate tension member (16) with atraumatic anchors (20) at each end. The member is 1-4 inches long between the anchors. The tension member may 0.01 - 0.02 inches diameter and 0.6 - 2.0 inches long. It may be a multi-filament with a radiopaque marker and an antithrombogenic coating. Alternatively it may be an echo cardiograph.

USE - Reducing the wall stress of a failing **heart** during **diastole** and **systole** .

ADVANTAGE - The device is a passive non-pharmalogical apparatus

that reduces the energy consumption of the failing **heart**.
DESCRIPTION OF DRAWING(S) - The figure shows a transverse cross-section of the left and right **ventricles** of a human **heart** showing the placement of a splint .
Elongate tension member (16)
Atraumatic anchors (20)
pp; 46 DwgNo 1/40
Derwent Class: B07; P31; P34
International Patent Class (Main): A61B-017/00; A61B-017/12; A61M-031/00

17/34/23 (Item 23 from file: 350)
DIALOG(R)File 350:Derwent WPIX

009072544 **Image available**
WPI Acc No: 1992-199963/199224
Copulsation and counter-pulsation **cardiac assist** appts. - uses train of pulses to activate each of the muscles in alternate fashion to **contract** respective muscles
Patent Assignee: UNIV MCGILL (UYMC-N)
Inventor: CHIU R C; CHIU R C J
Number of Countries: 016 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9208500	A1	19920529	WO 90CA390	A	19901109	199224	B
US 5429584	A	19950704	WO 90CA390	A	19901109	199532	
			US 9350392	A	19930818		

Priority Applications (No Type Date): WO 90CA390 A 19901109
Cited Patents: EP 216042; FR 2220279; FR 2321266; GB 1528072; US 4192293; US 4453537
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9208500	A1	E	15	A61M-001/12	
Designated States (National): CA JP US					
Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LU NL SE					
US 5429584	A		10	A61M-001/10	Based on patent WO 9208500

Abstract (Basic): WO 9208500 A
The copulsation and counterpulsation **cardiac assist** apparatus comprises copulsation and counterpulsation devices. The copulsation device includes a peri-**cardiac assist** device, including a fluid expansible envelope for compressing the **heart** during **systole** . The counterpulsation device performs a number of functions including a fluid expansible balloon for compressing a portion of the aorta during **diastole** . A muscle powered fluid pressure device supplies alternating fluid pressure to the copulsation and the counterpulsation devices. The **heart** rate is sensed and a stimulating pulse is produced to stimulate the selected muscles to **contract** . A reciprocating pump enables fluid pressure flows from one chamber to the other.
USE/ADVANTAGE - Combined peri-**cardiac** implant. Provides co-ordinated and combined totally implantable muscle powered peri-**cardiac** cup copulsation device.
Dwg. 1,2/6
Abstract (Equivalent): US 5429584 A

The co-pulsation and counter-pulsation **cardiac assist** appts. has a co-pulsation device including a peri-**cardiac assist** device with a fluid expansible envelope for compressing the **heart** during **systole** , and a counter-pulsation device comprising a peri-aortic **jacket** including a fluid expansible balloon for compressing a portion of the aorta during **diastole** . A muscle powered fluid pressure device supplies alternating fluid pressure to the co-pulsation and counter-pulsation devices.

A detector senses the **heart** rate and a pulse generator produces a stimulating pulse to selected muscles to **contract** them w.r.t. signals from the pressurising device. A negative pressure booster has adjacent separate flow chambers through which the alternating fluid pressures flow, and a reciprocating pump has at least a pump element in each chamber, such that when the fluid pressure flows through one chamber, it causes a pump to provide a negative pressure in the other chamber to enhance withdrawal of the fluid from a respective one of the co-pulsation and the counter-pulsation devices.

ADVANTAGE - Improved **heart** rate response control.

Dwg.2/6

Derwent Class: P33; P34; S05
International Patent Class (Main): A61M-001/10; A61M-001/12
International Patent Class (Additional): A61H-031/00

22/34/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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016818608
WPI Acc No: 2005-142891/200515
Implantable synthetic tissue or tissue complex useful for **treating heart** failure, myocardial infarct or disorder of bone, cartilage and ligament, comprises implantable synthetic tissue and another synthetic tissue
Patent Assignee: NAKAMURA N (NAKA-I)
Inventor: ANDO W; MATSUDA H; MIYAGAWA S; NAKAMURA N; SAWA Y; TAKETANI S; YOSHIKAWA H
Number of Countries: 108 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200512512	A1	20050210	WO 2004JP11401	A	20040802	200515	B

Priority Applications (No Type Date): JP 200458285 A 20040302; JP 2003285475 A 20030801
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200512512	A1	E	459	C12N-005/06	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

Abstract (Basic): WO 200512512 A1
NOVELTY - An implantable synthetic tissue (I) or a tissue complex

comprising an implantable synthetic tissue and another synthetic tissue.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing (M1) a synthetic tissue, involves providing cells, placing the cells in a container having cell culture medium comprising an extracellular matrix (ECM) synthesis promoting agent and having a sufficient base area which can accommodate a synthetic tissue having a desired size, culturing the cells in the container along with the cell culture medium containing the ECM synthesis promoting agent for a period of time sufficient for formation of the synthetic tissue having the desired size, and detaching the cells from the container, optionally regulating the thickness of synthetic tissue by physical or chemical stimulus to a desired thickness;

(2) a cell culture composition for producing a synthetic tissue from cells, comprising an element for maintaining the cells, and an extracellular matrix synthesis promoting agent;

(3) a complex (II) for reinforcing a portion of an organism, comprising cells and a component derived from the cells;

(4) reinforcing (M2) a portion of an organism, involves replacing the portion with a complex comprising cells and a component derived from the cells or providing the complex to cover the portion, or both, and holding the complex for a sufficient period of time for biologically adhering the complex to the portion;

(5) **treating** (M3) a portion of an organism, involves carrying out (M2); and

(6) a composition for use in producing synthetic tissue having a desired thickness, comprising a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents.

ACTIVITY - Cardiant; Vasotropic; Cardiovascular; Osteopathic. The ability of synthetic tissue to **treat** myocardial infarction was determined in vivo. The synthetic tissue was produced in the presence of ascorbic acids and was implanted into a **dialted** cardiomyopathy rat. The left anterior descending (LAD) was ligated for 2 weeks to produce injured **hearts**. The synthetic tissue was implanted into some of the injured **hearts**. As controls, rats without injury to their **hearts** were obtained. The rats were anesthetized and operated. The **heart** function of the rats was monitored on Day 14 and 28 after surgery. Two and four weeks after implantation, the rats were sacrificed with an excessive amount of pentobarbital. The **heart** was dissected, fixed with 10% formalin, and embedded in paraffin. A series of sections having a thickness of 5 mm were prepared. All of the rats with implants were completely cured, and survived for substantially the same period of time as normal rats. Therefore, it was demonstrated that the synthetic tissue can completely cure diseases in the presence of a specific ECM synthesis promoting agent.

MECHANISM OF ACTION - Cell-Therapy.

USE - (I) is useful for implantation of cells. (M2) is useful for reinforcing a portion of an organism, where the portion is a **heart** having a disease or disorder chosen from **heart** failure, ischemic **heart** disease, myocardial infarct, cardiomyopathy, myocarditis, hypertrophic cardiomyopathy, **dialted** phase hypertrophic cardiomyopathy and **dialted** cardiomyopathy. The portion includes avascular lesion, vascular lesion, bone, cartilage, intervertebral disk, meniscus, ligament or tendon, damaged or degenerated bone or cartilage, intractable fracture, osteonecrosis, cartilage injury, meniscus injury, ligament injury,

tendon injury, cartilage degeneration, meniscus degeneration, intervertebral disk denaturation, ligament degeneration or tendon degeneration. (M3) is useful for **treating**, **preventing**, or reinforcing a disease, disorder, or condition of **heart**, bone, cartilage, ligament, tendon, meniscus or intervertebral disk (all claimed).

ADVANTAGE - (I) is large sized, having a volume of 20 mm3, is flexible, **expand**able and **contract**ile, and can withstand **heart** pulsation (claimed). (I) is highly safe and does not cause any side effects when used in **treat**ment.

pp; 459 DwgNo 0/46

Technology Focus:

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Synthetic Tissue: (I) is biologically organized in the third dimensional direction. (I) has biological integration capability with surroundings, such as capability to adhere to surrounding cells and/or extracellular matrices. (I) comprises cells and is substantially made of cells and a material derived from the cells or ECM derived from the cells. The ECM contains collagen I, collagen III, vitronectin and fibronectin, preferably vitronectin and fibronectin. The ECM contains collagen I and collagen III, where the collagen constitutes 5-25% of the tissues, and the ratio of the collagen I to collagen III is between 1:10 and 10:1. The ECM and the cells are integrated together into a three-dimensional structure. The ECM is diffusedly distributed in the tissue and the distribution densities of the ECM in two arbitrary sections of 1 cm2 in the tissue have a ratio within a range of 1:3-3:1. (I) is heterologous, allogenic, isologous, or autogenous. (I) is free of scaffolds. (I) is biologically organized in all three-dimensional directions. The biological integration is chosen from internal **binding** of extracellular matrix, electrical integration, and intercellular signal transduction. (I) has a tissue strength, which allows the synthetic tissue to be clinically applicable. The strength is a break strength of 0.02-2 N. The tissue strength is sufficient to provide self-supporting ability, where the self-supporting ability is the capability of synthetic tissue to remain unbroken when the synthetic tissue is picked up using **force**ps having a tip area of 0.05-3 mm2, or with a hand. The site to which the synthetic tissue is intended to be applied includes **heart** , intervertebral disk, meniscus, cartilage, bone, ligament or tendon, where the synthetic tissue remains attached without an additional fixation procedure, after the synthetic tissue is implanted into an injured portion of the intra-articular tissue. In (I), the implantable synthetic tissue is biologically integrated with the other synthetic tissue by an extracellular matrix.

Preferred Method: In (M1), the stimulus for inducing tissue **contraction** is applied in the detaching step. The stimulus includes a physical or chemical stimulus. The physical stimulus includes shaking of the container, pipetting or deformation of the container. The detaching step includes adding an actin regulatory agent, which comprises a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents. The actin depolymerizing agent is chosen from Slingshot, cofilin, cyclase associated protein (CAP), actin interacting protein 1 (AIP1), actin depolymerizing factor (ADF), destrin, depactin, actophorin, cytochalasin and nerve growth factor (NGF). The actin polymerizing agent is chosen from RhoA, mDi, profilin, Rac1, IRSp53, WAVE2, ROCK, LIM kinase, cofilin, cdc42, N-WASP, Arp2/3, Drf3, Mena, lysophosphatidic acid (LPA), insulin, platelet derived growth factor-a ((PDGF)-a), PDGF-b, chemokine and transforming growth

factor (TGF)-(beta). The chemical stimulus is obtained by using a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents. The container is free of scaffolds. The cells are first cultured in monolayer culture. The ECM synthesis promoting agent includes TGFbeta1, TGFbeta3, ascorbic acid, ascorbic acid 2-phosphate, or its derivatives or salts. The ascorbic acid, ascorbic acid 2-phosphate, or its derivative or salt is present at a concentration of 0.1 mM. The TGFbeta1 or TGFbeta3 is present at a concentration of 1 ng/ml. The cells are placed at a concentration of 5x10 to the power 4-5x10 to the power 6 cells/cm squared. (M1) further involves causing the synthetic tissue to detach from the container and self-**contract**, and causing the synthetic tissue to differentiate, where the detaching and self-**contract**ion are achieved by providing a physical stimulus or chemical stimulus to the container. The culturing step is carried-out for a sufficient period of 3 days and a period of time required for the synthetic tissue to be spontaneously detached from the container at a maximum, which is at least 40 days. The differentiation includes osteogenesis, chondrogenesis, adipogenesis, tendon differentiation and ligament differentiation. The osteogenesis is performed in medium containing dexamethasone, beta-glycerophosphate and ascorbic acid 2-phosphate. The medium contains any one of bone morphogenetic protein-2 (BMP-2), BMP-4, BMP-7, TGF-beta1 and TGF-beta3. The chondrogenesis is performed in medium containing pyrubic acid, dexamethasone, ascorbic acid 2-phosphate, insulin, transferring and selenious acid. The differentiation step is performed before or after the detaching step, preferably after the detaching step. The cell includes cells of 3 or more passages, preferably 3-8 passages. The cells include myoblasts, fat-derived cells, synovium-derived cells and mesenchymal stem cells, which are derived from an adipose tissue, synovial membrane, a tendon, bone or bone marrow. (M1) further involves producing several synthetic tissues and attaching the synthetic tissues together to be integrated. The desired thickness is regulated by adjusting a ratio of the actin depolymerizing agent to the actin polymerizing agent. In (M2), the ECM is provided on a surface of the complex, or diffusedly distributed on a surface of the complex. (M2) further involves forming the complex by culturing the cells in the presence of an ECM synthesis promoting agentand implanting another synthetic tissue. In (M2), the complex is held for a sufficient period of time, which is at least 10 days. The other synthetic tissue is an artificial bone or a microfibrous collagen medical device. The complex is substantially made of cells and an ECM derived from the cells. The artificial bone includes hydroxyapatite.

Preferred Complex: In (II), the portion includes avascular tissue, intravertebral disk, meniscus, ligament or tendon. The rein**force**ment is achieved by replacing the portion with the complex or providing the complex to cover the portion, or both. (II) **resists** the **expansion** and **contract**ion of the portion.

Extension Abstract:

EXAMPLE - No relevant example is given.

Derwent Class: B04; D16; D22
International Patent Class (Main): C12N-005/06

22/34/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013843223 **Image available**
WPI Acc No: 2001-327436/200134
Passive **girdle** includes **wrap** member with con**straining** material that **resists** **heart** **expansion** beyond one of preset inner perimeters or **wrap** member without **resisting** **systolic** ejection
Patent Assignee: ABIOMED INC (ABIO-N)
Inventor: KUNG R T V; LEDERMAN D M
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 6224540	B1	20010501	US 95490080	A	19950613	200134	B
			US 95581051	A	19951229		
			US 9823592	A	19980213		

Priority Applications (No Type Date): US 95581051 A 19951229; US 95490080 A 19950613; US 9823592 A 19980213
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 6224540	B1		10	A61F-002/04	CIP of application US 95490080
					Div ex application US 95581051
					CIP of patent US 5713954
					Div ex patent US 5800528

Abstract (Basic): US 6224540 B1
NOVELTY - The **girdle** (17) includes a **wrap** member that conformingly surrounds at least a portion of the circumference of the **heart** (10). The **wrap** member provides a passive sustained dimensional **constraint** on a **heart** muscle. The con**straining** material is adjustable to **resist** **expansion** of the **heart** beyond one of the predetermined inner perimeters of the **wrap** member without **resist**ance to **systolic** ejection.
USE - Used for **heart** **ventricle** to provide therapeutic **aid** to patients having **ventricular** **dialt**ation.
ADVANTAGE - Enables **girdle** to be adjustable in size and **shape** over extended period of time to gradually decrease **ventricular** **dialt**ation. Employs fluid filled passive **wrap** that provides for variable volume to be enclosed by **wrap** . Provides feedback system wherein sensors can be built into **indistens**ible lining to measure its tension, thereby providing automatic feedback to hydraulic circuit controlling **wrap** volume. Employs tissue engineered lining to protect myocardium.
DESCRIPTION OF DRAWING(S) - The figure is the cross-sectional view of the passive **girdle**.
Heart (10)
Girdle (17)
pp; 10 DwgNo 1/7
Derwent Class: P32
International Patent Class (Main): A61F-002/04

24/34/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012077694 **Image available**

WPI Acc No: 1998-494605/199842
Method of **treat**ing patient with **heart** having **ventricular dialt**ion - involves use of **girdle**, formed of material and structure that does not **expand** away from **heart**, which is **wrap**ped around **heart** muscle
Patent Assignee: ABIOMED R & D INC (ABIO-N)
Inventor: KUNG R T V; LEDERMAN D M
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5800528	A	19980901	US 95490080	A	19950613	199842	B
			US 95581051	A	19951229		

Priority Applications (No Type Date): US 95581051 A 19951229; US 95490080 A 19950613
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5800528	A		9	A61F-002/04	CIP of application US 95490080

Abstract (Basic): US 5800528 A

The method for **treat**ment of a patient, whose **heart** is characterized by **ventricular dialt**ation comprises the steps of, **wrap**ping a **girdle** around at least the **ventricle** of the patient's **heart**. The **girdle** is **wrap**ped such that it can adjust in size and **shape** to facilitate a gradual reduction in the size of the **heart**. The method then involves maintaining the **girdle** in a passive state for an extended period of time. The **girdle** in the passive state conforms to the outer **shape** of the **ventricle** and does not **expand** its dimension in a direction away from the natural **heart**.

The **girdle** is formed of a sheet of material prestressed in the plane of the sheet to a value below the elastic **limit** of the material, the sheet having a tension which **limits** extension away from the **heart** , while providing compression **forces** radially inward toward the **heart** .

ADVANTAGE - Improves performance characteristics of the **heart**.

Dwg.1b,4/7
Derwent Class: P32
International Patent Class (Main): A61F-002/04